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03-1327
(Serial No. 08/485,129)

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

IN RE DAVID WALLACH, HARTMUT ENGELMANN,
DAN ADERKA, DANIELA NOVICK, and MENACHEM RUBINSTEIN

Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences

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REPLY BRIEF FOR APPELLANTS

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CORRECTED

CERTIFICATE OF INTEREST

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

IN RE WALLACH v. _____

No. 03-1327

Certificate of Interest

Counsel for the ~~(petitioner)~~ (appellant) ~~(cross-appellant) (respondent) (appellee) (amicus) (name of party)~~ Wallach et al certifies the following (use "None" if applicable; use extra sheets if necessary):

1. The full name of every party or amicus represented by me is:

David Wallach, Hartmut Engelmann, Dan Aderka, Daniela Novick and Menachem Rubinstein

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

Yeda Research and Development Co. Ltd.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

None

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

None

April 24, 2003
Date

Signature of counsel

Roger L. Browdy
Printed name of counsel

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ARGUMENT

I. Granting of This Patent Will Not Chill Research in Recombinant DNA Techniques

The Solicitor makes the alarmist argument at page 29 of the brief:

> Put another way, if Wallach's argument were accepted, then every time someone isolated a protein in nature, that person would then be entitled to patent claims to every DNA molecule that could be used to genetically manufacture that protein without ever having any knowledge of those DNA molecules. If that were true, there would be no incentive for any inventor to develop materials and methods for the production of proteins using recombinant DNA techniques.

This "sky is falling" argument does not withstand closer scrutiny. Allowance of the present claims will no more serve as a disincentive to development of materials and methods for the production of the TBP-II using recombinant techniques than would the issuance of the patent on the protein claims, which are admittedly allowable. A patent on the protein covers the protein however produced. Thus, that patent would dominate the production of that protein by recombinant techniques. Anyone seeking to produce the patented protein by recombinant techniques would need to seek a license from the patentee.

Similarly, the present claims, drawn to the genus of DNA sequences encoding that protein, would dominate a technique using the natural cDNA sequence. However, this does not mean that inventors who develop the materials for the production of the protein using recombinant DNA techniques could not get their own patent on the cDNA. Appellants do not argue here that

individual natural cDNA sequences would have been obvious from a disclosure of the protein. Yes, the present claims would dominate any patent obtained on the cDNA, but this would not eliminate incentive for inventors to develop materials and methods for the production of proteins using recombinant DNA techniques any more than would the existence of patents on the protein *per se*.

It is Appellants' position that the isolation and description of a novel protein by means of partial amino acid sequence and other characterizing disclosure, as is the case here, puts one in possession of that protein, including its inherent amino acid sequence. That inherent amino acid sequence implicitly includes the disclosure of the genus of DNA sequences that encode that amino acid sequence, which may be deduced therefrom.

II. *In re Deuel* Is Not Dispositive

The Solicitor argues that this court's decision in *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995) forecloses Wallach's position that disclosure of a partial amino acid sequence adequately describes the DNA molecules encoding a particular protein (page 23). However, the Solicitor's quotation from *Deuel* at pages 22 and 23 of the Brief leaves out the important sentence which concludes the quoted paragraph and reads:

> We will therefore reverse the final rejection of claims 4 and 6 because neither the Board nor the patent examiner articulated any separate reasons for holding these claims unpatentable apart from the grounds discussed above.

It is evident that the issues were not fully developed on this point in *Deuel* and, thus, these claims were left to stand or fall with the remaining claims directed to a specific cDNA. This is hardly a ruling that could be determined to be the final word on the subject. If the reasoning and arguments presented herein had been presented by the Solicitor in the *Deuel* case with respect to claims 4 and 6, the Court could and should have arrived at a different conclusion. As the issues were admittedly not developed in *Deuel*, *Deuel* should not permit the achievement of a different resolution on consideration of the fully developed issues.

III. Granting of the Present Claims Would Not Be Repugnant to Currently Accepted Biotechnology Patent Practice

At pages 29 and 30 of the Solicitor's brief, the Solicitor states that claims to DNA molecules encoding known isolated proteins that were not held invalid or obvious over prior art in previous cases would now be held anticipated or obvious. Among the cited cases are *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991), *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993) and *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997). These statements are not entirely accurate.

In the *Eli Lilly* case, the claims were explicitly directed to cDNA, i.e., the single DNA sequence that corresponds to the natural sequence of the mRNA that encodes the protein. While the claims of *Amgen* and *Fiers* were not specifically directed to cDNA, the parties argued the issues, and the court

decided the issue as if they were. Note in *Amgen* the court stated, 927 F.2d at 1206:

> We hold that when an inventor is unable to envision the detailed chemical structure of the gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated. [emphasis added]

The court's determination in *Amgen* that one has not conceived of the sequence of a "gene" until he has obtained it is fully applicable to the natural sequence of the naturally-occurring gene that encodes the protein in question.

Similarly, in *Fiers* the court referred to "the complete nucleotide sequence of the DNA coding for β-IF"[1] [emphasis added]. The term "the DNA" suggests that there is only one sequence coding for β-IF. Clearly, the parties and the court had in mind the sequence of the gene or the cDNA, i.e., a very particular sequence, not the genus of DNA that anyone could obtain by means of the amino acid sequence with a computer. The holdings of *Amgen* and *Fiers* that one cannot conceive of a sequence until he obtains it would not be applicable to a claim that reads on the genus of all DNA sequences that encode a protein of known amino acid sequence. The Solicitor's brief does not dispute Appellants' point that anyone with a computer could write out every sequence that encodes any particular amino acid sequence. Accordingly, ruling for Appellants here would

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[1] 984 F.2d at 1168.

not be repugnant to currently accepted biotechnology patent practice.

Far from being repugnant to currently accepted biotechnology patent practice, a ruling in Appellants' favor would serve the public policy and the Constitutional objective of promoting technical progress. Both are advanced when patent applications are filed as soon as the inventor can provide an enabling disclosure for practicing an invention. Indeed, this court has stated on more than one occasion, "[e]arly publication disclosure is a linchpin of the patent system." *W. L. Gore & Asso., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1550 (Fed. Cir. 1983), cited in *OddzOn Products Inc. v. Just Toys Period Inc.*, 122 F.3d 1396, 1402 (Fed. Cir. 1997). Appellants here have made an early public disclosure of a newly-discovered protein. As the DNA sequence can be readily deduced from the sequence of the protein, Appellants have demonstrated that they were as much in possession of that sequence as they were in possession of the protein itself, including its inherent amino acid sequence, at the time that the application was filed. Thus, Appellants were in possession of the novel protein and the corresponding genus of DNA sequences at the time of their early disclosure by means of a patent application. Such should be encouraged and not held repugnant.

IV. The Solicitor Misquotes *Eli Lilly*

On page 18 of the Solicitor's brief, the Solicitor states:

> However, a generic statement that a genus of DNA molecules encodes a particular protein "without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others ... it is only an indication of what the [genus of DNA molecules] does, rather than what it is." *Eli Lilly*, 119 F.3d at 1568 (emphasis added); ...

However, *Eli Lilly* was not talking about a genus of DNA molecules encoding a single protein. *Eli Lilly* was talking about a genus of specific cDNA sequences of different species. The full quote reads as follows:

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.
>
> A genus of vertebrate insulin cDNA or mammalian

insulin cDNA is quite different from the present genus. Knowing one species in the genus of the *Eli Lilly* case does not put one in possession of any other species as each of the sequences is unique. Each cDNA in that genus encodes a different amino acid sequence. On the other hand, the genus of DNA that encodes a single protein is quite different because, if one is in possession of any sequence within the genus, one is in

possession of them all. Each member of the genus has in common that it encodes a single specific protein. The fact that it encodes a single protein describes what the genus is. All members of the genus define the same protein, and all can be determined by the genetic code without any additional experimentation. That is not the situation in *Eli Lilly* where one must painstakingly find by experimentation the cDNA for each vertebrate insulin. Only the DNA that encodes the human TBP-II protein is here being claimed.

In *Enzo Biochem Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324-1325 (Fed. Cir. 2002), this court stepped back from the harsh statements of prior cases, implying that a DNA molecule could not be claimed without disclosure of the entire sequence, and adopted the standard that the written description requirement can be met by showing that an invention is complete by disclosure of sufficiently detailed relevant identifying characteristics, such as partial structure, other physical or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure or some combination of such characteristics. Here the Solicitor has conceded at page 14, lines 2-5, that the Wallach specification includes a predicted 30 nucleotides of the sequence, i.e., there is disclosure of a partial nucleotide sequence. The Solicitor further concedes at page 4, lines 2-4, that the Genetic Code makes it possible to predict which DNA molecules can encode a protein if the amino acid sequence of that protein is known.

Thus, the present DNA genus is defined by a partial sequence and the known correlation of the structure of the DNA, which can be readily converted to the amino acid sequence it encodes, and the detailed characterizations of the function of that amino acid sequence (protein). This is fully consistent with *Eli Lilly* as interpreted in the *Enzo* case.

V. The Function of a DNA Sequence Can Be Defined by the Function of the Protein

The Solicitor often repeats the statement that Wallach's specification does not teach any function of the claimed DNA molecules except "the naked recitation that they encode the TBP-II protein". See for example page 2, line 2, page 6, line 5, and page 19, line 8, of the Solicitor's brief. However, it is not understood why this statement is minimized or considered to be "naked". This recitation is clothed in the disclosed recitations of the properties of the protein. Any given DNA sequence could be tested for compliance with this claim by simply converting the codons thereof to amino acids by means of the genetic code and then applying the same test that would apply if one were analyzing the protein claim. Because there is a one-to-one correspondence of a given DNA sequence with its corresponding amino acid sequence, a recitation of the functions of the protein is sufficient to flesh out the functions of the DNA molecule that encodes it.

Similarly, the Solicitor states that the Wallach specification fails to provide any other information from which the claimed DNA molecules might be distinguished from other DNA

molecules. However, the Solicitor concedes that 7% of the sequence is disclosed. This partial sequence, in combination with the properties of the protein identified by the amino acid sequence that can readily be deduced from the nucleotide sequence is more than sufficient to distinguish the claimed DNA molecules from other DNA molecules.

The Solicitor states that claim 11 is silent about the structure of any other portions of the DNA molecules that might appear in the full-length TBP-II protein but which may be necessary for proper expression of the TBP-II protein, e.g., a signal sequence. However, claim 11 is not a claim to an expression vector. It is only directed to the coding sequence, which is in the nature of a sub-combination of an expression vector. While a vector claim might need to include everything required for proper expression, this is not a requirement of a DNA claim. Claim 11 only requires that the DNA encode the mature TBP-II protein described in the specification. The Solicitor's reference to portions of DNA other than that claimed appears to be irrelevant.

The Solicitor states at page 11 of the brief that Wallach's line of reasoning is inconsistent with the current state of law, which permits patents for DNA molecules that encode a given protein when the protein is known in the prior art. Appellants' line of reasoning is not inconsistent with the current state of the law that permits patents for cDNA molecules that encode a given protein when the protein is known in the prior art. The current state of the law has never fully

analyzed the issue of whether generic claims to all DNA sequences, which can readily be determined by the genetic code from the sequence of the protein, may be patentable. Decision for Appellants in this case would not affect the ability of a subsequent inventor in obtaining a patent on the specific cDNA that encodes TBP-II. The natural cDNA sequence is not necessarily obvious from the genus of all possible DNA sequences that can encode the protein. The natural sequence cannot be envisioned until that cDNA is isolated an analyzed. However, the genus of DNA can be envisioned merely from knowledge of the amino acid sequence. The fact that Appellants' specification does not disclose the complete amino acid sequence, but only a partial amino acid sequence and sufficient characterizing information to put one of ordinary skill in full possession of a novel protein, should not change the result as the amino acid sequence is an inherent property of that protein that is in the possession of Appellants, and the genus of DNA that corresponds thereto is merely a different language for saying the same thing, i.e., defining that amino acid sequence.

The DNA sequence in this case is nothing but a method of writing the amino acid sequence in a different language. Thus, the simplest amino acid sequence is a single residue. If that residue is methionine, the genetic code says the corresponding DNA codon is ATG. If one says to a molecular biologist "the codon ATG", that molecular biologist will immediately think "methionine." "Methionine" and "the amino acid encoded by ATG" are one and the same.

Similarly, Thr and the DNA codon ACN, where N is A or G or C or T, are one and the same. Thus, "the amino acid sequence encoded by ATG-ACN" is merely another way of saying Met-Thr. The DNA sequence "ATG-ACN" is a genus of the four sequences ATG-ACT, ATG-ACC, ATG-ACA and ATG-ACG. However, what this genus of sequences has in common is that each species encodes Met-Thr. There is a one-to-one correspondence between every species of DNA within that genus and the single specified amino acid sequence Met-Thr. If Met-Thr were a dipeptide that had a certain physiological function and the specification disclosed that dipeptide and its function and merely stated that the invention also included all those DNA sequences that encoded Met-Thr, there would be no question that there was sufficient written description for the four DNA sequences in this genus. The same reasoning applies no matter how large the amino sequence acid is.

This exercise is merely intended to establish that when one is defining an amino acid sequence using a different language, one is still defining the amino acid sequence. Therefore, the function of the protein encoded by the amino acid sequence is as relevant to the DNA sequence as it is to the amino acid sequence. This is not a mere "naked" recitation, but an important disclosure of function. It is not believed that the Solicitor would take the position that the person who finished the sequencing of the TBP-II protein first isolated by the present Appellants would be entitled to a patent on the complete amino acid sequence. Protein claims have already been

found to be allowable from the present disclosure. The complete amino acid sequence is an inherent feature of the protein, and when the protein is fully disclosed by partial amino acid sequence and other characterizing features, then the protein is sufficiently described and, absent prior art, is allowable. Thus, the inherent amino acid sequence is no longer patentable. The recitation of every DNA sequence that encodes that amino acid sequence is merely another way of reciting that sequence in another language. It should be considered to be in the possession of the present Appellants to the same manner that the inherent amino acid is in the possession of the present inventors.

CONCLUSION

Enzo Biochem Inc. v. Gen-Probe Inc., *supra*, adopted the standard that the written description requirement can be met by showing that an invention is complete by disclosure of sufficiently detailed relevant identifying characteristics, such as partial structure, other physical or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure or some combination of such characteristics. Here the Solicitor has conceded at page 14, lines 2-5, that the Wallach specification includes a predicted 30 nucleotides of the sequence, i.e., there is disclosure of a partial nucleotide sequence. The Solicitor further concedes at page 4, lines 2-4, that the Genetic Code

makes it possible to predict which DNA molecule can encode a protein if the amino acid sequence of that protein is known.

The genus of DNA sequences, each species of which encodes the amino acid sequence of TBP-II, which sequences can be readily deduced from the amino acid sequence, is as much an inherent property of the protein as is its amino acid sequence. One can readily determine whether any given DNA sequence falls within the scope of the claims by first looking for the 30 nucleotides effectively defined in the claim, and if present, then converting the nucleotide codons to amino acid residues and determining if the polypeptide so obtained has the functional properties defined in the claim. As Appellants are in possession of the protein, Appellants are also in possession of the genus of nucleotide sequences that encodes such a protein.

Reversal of the Board's decision is, therefore, earnestly solicited.

Respectfully submitted,

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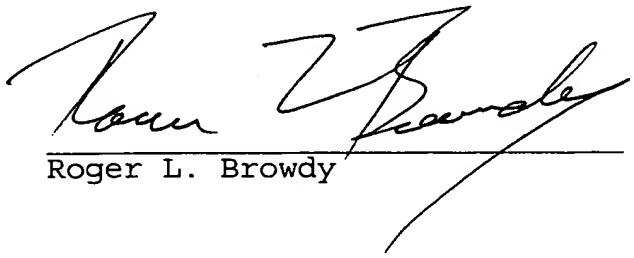
PROOF OF SERVICE

I hereby certify that a true copy of the foregoing **CORRECTED REPLY BRIEF FOR APPELLANTS** was mailed by depositing with the U.S. Postal Service, with sufficient postage as First Class Mail, addressed to Mary L. Kelly, Esq., Office of the Solicitor, P.O. Box 15667 Arlington, VA 22215, on this 13th day of November, 2003.

Roger L. Browdy

CERTIFICATE OF COMPLIANCE

I hereby certify that the present brief complies with the type-volume limitation of FRAP 32(a)(7)(B)(i). The word count of the word processing system used to prepare the brief shows a total of 3731 words, including the Table of Contents, Table of Citations and Statement of Related Cases, as well as this Certificate of Compliance, which need not have been counted in the type-volume limitation. Thus, the portion of the brief which must be counted must contain no more than 7,000 words.



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